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REMARKS

Claims 1-66 are pending. Claims 23-58, and 64-66 are withdrawn from consideration. Claims 1-22 and 59-63 are rejected. Claims 1 and 6 have been amended, as supported by the disclosure at by page 5, line 22; page 13, line 20; and page 23, line 15. Claims 1-66 remain in the case.

Applicants would like to thank Examiner Sorkin for the courtesy of an interview on January 14, 2002. The interview was very helpful in advancing a mutual understanding of the issues in the present case.

Claims 1-22 and 59-63 are rejected under the second paragraph of Section 112. The examiner urges that the phrase "rooted in pores" is indefinite, as it is unclear what scope of structures this phrase includes." Applicants have amended claims 1 and 6 to recite that the polymer is "crosslinked inside the pores," as supported by the disclosure at pages 5, 13, and 23. Reconsideration and withdrawal of the rejection under the second paragraph of Section 112 are respectfully requested.

Claims 1-10, 13-22, and 59-63 stand rejected under Section 103(a) based on Carr *et al.*, and claims 1-22 and 59-63 stand rejected under Section 103(a) based on Carr *et al.* in view of Girot *et al.* The examiner states that:

the lowest porosity explicitly disclosed is 31%, which occurs at a sintering temperature of 900 degrees. It is considered that it would have been obvious to one of ordinary skill in the art to have made the porosity < 30%. Carr *et al.* ('373) discloses that "the surface area and pore volume decrease with increasing firing temperature" (col. 13, lines 37-39) and also that the sintering temperature can range for 100-1500 degrees (col. 8, lines 20-29). This would suggest to one of ordinary skill in the art to decrease the porosity below 30%.

When considered in its entirety, however, the disclosure of Carr *et al.* would not have led one of ordinary skill to decrease porosity, or pore volume, below 30%. Carr *et al.* teaches that at least *two* parameters affect pore volume and pore diameter: firing temperature ("the surface area and pore volume decrease with increasing firing temperature") and colloid size ("larger colloids produce fired spherules with larger pore diameters and pore volumes" - col. 14, lines 4-5). Thus, pore volume can be decreased by increasing the firing temperature or by decreasing the colloid size. Conversely, the two

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parameters can be selected so that they counteract one another, *i.e.*, a higher firing temperature could be used with a larger colloid size to increase surface area (as a result of the higher firing temperature) and pore diameter (as a result of the larger colloid size), *without* decreasing pore volume. The question is whether Carr *et al.* suggests that the *desirability* of decreasing the pore volume below the 31% that is disclosed.

When Carr *et al.* is read as a whole, the clear message is that pore volume should be maximized, and not controlled to values of less than 30% as presently claimed. Increased pore diameter and pore volume both allow more of the proteins which are to be separated to diffuse freely into the internal void volume, thereby reaching all available surface area, which also should be maximized. Thus, Carr *et al.* states that "the data summarized in Table 1 show that it is possible to increase the average pore diameter by increasing the firing temperature from 400° to 900°C. The surface area and pore volume decrease with increasing firing temperature. *Chromatographic activity of the ZrO₂ spherules is determined by the parameters of the surface area, average pore diameter and pore volume. Accordingly, the appropriate firing temperature is selected*" (column 13, lines 35-42, emphasis added).

Similarly, Carr *et al.* discloses that a colloid size should be chosen which maximizes both pore volume and pore diameter. For example, Carr *et al.* states that "the data summarized in Table II show that it is possible to control the average pore diameter of the fired spherules by appropriate selection of the colloid size of the ZrO₂ source. Larger colloids produce fired spherules with larger pore diameters and pore volumes" (column 14, lines 1-5).

The examples of Carr clearly select firing temperature and colloid size so as to maximize porosity and pore size, typically by using a firing temperature of 600°C. A further emphasis on increasing both pore volume and pore size is found in Example 8, which discloses that "centrifugation, removal of the supernatant, and redispersion of the colloidal ZrO₂ starting material results in increases in the average pore diameter, pore volume and surface area of the fired spherules...regardless of mechanism, the centrifugation treatments described in Examples 6-8 provide a method of preparing spherules with

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increased average pore diameter, *pore volume* and surface area relative to spherules prepared from untreated colloidal ZrO₂ sols" (column 16, lines 13-17, emphasis added).

The examples which relate to coated particles all use particles prepared according to Example 2. Example 2 fires the ZrO₂ spherules at 600°C. As shown in Table 1, these particles have a pore volume of 36%. There is no suggestion to fire at a higher temperature in order to reduce this pore volume. Indeed, as noted above, the clear suggestion in Carr *et al.* is that both pore volume and pore size should be maximized. Accordingly, there is no suggestion to modify the firing temperature to be used in order to produce a matrix with a pore volume of less than 30% as presently claimed.

Indeed, a modification of Carr *et al.* to decrease pore size and volume would be contrary to the teaching of the reference, which seeks to maximize the access of proteins to the interior of the matrix. If a proposed modification renders a prior art invention unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. "The question is . . . whether it would have been obvious from a fair reading of the prior art reference as a whole to . . . [modify the reference] . . . The mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification." *In re Gordon*, 221 USPQ 1121, 1127 (Fed. Cir. 1984). See also MPEP §2143.01. In analyzing the prior art, it is impermissible to "pick and choose from any one reference only so much of it as will support a given position, to the exclusion of the other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). "Whether a particular combination might be 'obvious to try' is not a legitimate test of patentability." *In re Fine*, 837 F.2d 1071, 1075 5 USPQ2d 1596, 1599 (Fed. Cir. 1988).

Applicants produce particles with low pore volume by firing at high temperatures, in the range of 900°C to 1500°C, and preferably between 1000°C and 1400°C, so as to melt the submicroparticles together and reduce the particle diameter and reduce the pore volume to less than about 30%. This low pore volume material is essential to firmly anchor the interactive polymer network on the beads - to provide a polymer network that is firmly rooted in the pores. Carr *et al.* teaches away from a pore volume of less than 30%

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as recited in applicants' claims. As a general rule, a prior art reference that teaches away cannot serve to create a *prima facie* case of obviousness. *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). Regarding teaching away, a prior art reference is said to teach away from the claimed invention when "a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *Id.* Teaching away is a *per se* demonstration of lack of *prima facie* obviousness. *In re Dow*, 5 USPQ2d 1596 (Fed. Cir. 1988). The path taken by applicants diverges from that suggested of Carr et al., by using a mineral oxide matrix with a pore volume of less than 30%.

The issue of obviousness is determined entirely with reference to a hypothetical person having ordinary skill in the art. *Standard Oil Co. v. American Cyanamid Co.*, 774 F.2d 448, 454, 227 USPQ 293, 297-98 (Fed. Cir. 1985). Furthermore, in considering the person of ordinary skill in the art, that hypothetical person is "presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate" *Id.* Therefore, persons of ordinary skill are guided by conventional wisdom. *W.L. Gore & Assoc.*, 721 F.2d 1540, 1553, 220 USPQ 303 (Fed. Cir. 1983). In *Carr et al.*, the "conventional wisdom" is to increase porosity, not to make a mineral oxide matrix which has a pore volume of less than 30%.

In summary, the emphasis in Carr is on large pore diameters and pore volume, to allow free access to the interior of proteins to be separated. In clear contrast, the present invention uses a pore volume of less than 30%, one that is "just large enough to allow polymers to be rooted in the pores." Applicants' claimed pore volume is intrinsically related to its purpose of firmly anchoring an interactive polymer network that is crosslinked in the pores. The interaction of the desired molecules occurs on the external surface area of the beads due to the rooted polymers. Thus, in applicants' support, a surface layer of polymer that can interact with desired macromolecules and that is held stably in place because it is part of a network that is crosslinked in the pores of the media. This is described in the paragraph bridging pages 9 and 10 of the specification:

the pore volume is left just large enough to allow polymers to be rooted in the pores, and these rooted polymers layer on the external surface of the

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beads where the interaction with the macromolecules occurs. The resulting layer of polymers, or interactive polymer network, is stable and remains in place. The interaction of the desired molecules occurs on the external surface area of the beads due to the rooted polymers.

Giroi *et al.* is added for a teaching of polysaccharide organic polymers as the material of the polymer network. Giroi *et al.* does not overcome Carr's failure to suggest a matrix with a pore volume of less than 30% in which an interactive polymer network is crosslinked. Reconsideration and withdrawal of the rejections under Section 103(a) are requested.

In view of the foregoing remarks, it is believed that all claims are in condition for allowance. Reconsideration of all rejections and a notice of allowance are respectfully requested. Should there be any questions regarding this application, the examiner is invited to contact the undersigned attorney at the phone number listed below.

Respectfully submitted,

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